Monoamine oxidase A distribution volume as a correlate for electroconvulsive therapy – preliminary results

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Aim of the study
Electroconvulsive therapy (ECT) is an effective treatment option in major depressive disorder (MDD) and treatment-refractory depression. Despite its undoubtedly effectiveness and its widespread use, the underlying neurobiological mechanisms are still not fully understood. Preclinical and clinical findings particularly emphasize an involvement of the serotonergic neurotransmitter system in its mode of action [1]. Previously, our group showed that ECT was accompanied by a global downregulation of the postsynaptic serotonin-1A receptor [2]. As of now, the aim of this ongoing study is to assess the effect of ECT on the monoamine oxidase A (MAO-A), the major serotonin degrading enzyme, which – in accordance with the monoamine theory of depression – was shown to be elevated in MDD patients [3]. Preliminary data of four patients are shown here.

Patients and Methods
Four subjects (3 female, aged 47 ± 3.61 years, 1 male, aged 25 years) with severe unipolar depression determined by the Structural Clinical Interview for DSM IV and the 17-item Hamilton Rating Scale for Depression (HAM-D17 score ≥ 23) participated in this neuroimaging study. ECT was carried out unilaterally (right-sided) according to international standard operating procedures. Antidepressant medication was in steady-state for ten days prior inclusion and was administered in unchanged dosage during study participation. Patients underwent two positron emission tomography (PET) scans using the radioligand [11C]charmione, one before and one after eight ECT sessions. PET images were co-registered to structural magnetic resonance imaging scans and normalized using SPM12. MAO-A distribution volume (VMAO) maps were calculated voxel-wise in PMOD 3.509 with the Logan plot using arterial input functions and the thalamus time activity curve as input.

Results
Paired t-test using the global MAO-A VMAO of 47 brain regions including dorsal and medial raphe nucleus (AAL atlas [4]), averaged for both hemispheres and corrected for size, revealed a significant difference across the brain (t = 4.161, p = 0.0252), showing a decrease of MAO-A VMAO following ECT in four depressed patients. When considering regional paired t-test, significant differences could be noticed in 25 out of 47 regions, e.g. the anterior cingulate cortex (p = 0.009), posterior cingulate cortex (p = 0.007), the inferior frontal gyrus (p = 0.009) and the dorsal raphe nucleus (p = 0.026, all uncorrected).

Conclusion
These preliminary findings implicate a reduction of MAO-A VMAO following treatment with ECT. This would be in accordance with previous data showing increased MAO-A VMAO in MDD compared to healthy subjects [3], based on the assumption that the healthy condition resembles the post-ECT condition and the depressed condition the pre-ECT condition, respectively. Therefore, one might carefully interpret that ECT leads to a “normalization” of MAO-A levels in depressed patients. However, these data represent only preliminary findings of four patients in an ongoing PET study and the small size must be considered when interpreting the results.

References

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Figure
Regional monoamine oxidase A (MAO-A) distribution volume (VMAO) on a triplanar view, superimposed on a single-subject MRI standard structural magnetic resonance image quantified using the radioligand [11C]charmione. The figure displays MAO-A VMAO of four depressed patients before and after a unipolar ECT sessions, largely showing a clear reduction of MAO-A VMAO after ECT. The color bar indicates MAO-A VMAO.